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Docket No. 62812-A/JPW/GJG/CSN

APR 25 2002

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Applicants : Mitchell Shirvan and Meir Bialer  
Serial No. : 09/932,370  
Filed : August 17, 2001  
For : USE OF DERIVATIVES OF VALPROIC ACID AMIDES AND  
2-VALPROENIC ACID AMIDES FOR THE TREATMENT OR  
PREVENTION OF PAIN AND/OR HEADACHE DISORDERS.

1185 Avenue of the Americas  
New York, New York 10036  
April 15, 2002

Assistant Commissioner for Patents  
Washington, D.C. 20231

SIR:

**INFORMATION DISCLOSURE STATEMENT**  
**PURSUANT TO 37 C.F.R. §1.97(b) (3)**

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following publications which are listed again on the attached Form PTO-1449 (**Exhibit A**) and copies of the references as **Exhibits 1-28** are enclosed in connection with the above-identified application.

This Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b) (3).

1. U.S. Patent No. 4,639,468, issued January 27, 1987 (Roncucci et al.) (**Exhibit 1**);

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2. U.S. Patent No. 4,913,906, issued April 3, 1990 (Friedman et al.) (**Exhibit 2**);
3. U.S. Patent No. 5,585,358, issued December 17, 1996 (Bialer et al.) (**Exhibit 3**);
4. U.S. Patent No. 5,945,416, issued August 31, 1999 (Shannon et al.) (**Exhibit 4**);
5. U.S. Patent No. 6,251,946, issued June 26, 2001 (Vinikova et al.) (**Exhibit 5**);
6. U.S. Patent No. 6,268,396, issued July 31, 2001 (Nau et al.) (**Exhibit 6**);
7. Belgian Patent Application No. 885.303, published September 19, 1980 (Roncucci et al.) (**Exhibit 7**);
8. Canadian Patent No. 1 208 230, issued July 22, 1986 (Chambon et al.) (**Exhibit 8**);
9. European Patent Application No. 0 046 707, published March 3, 1982 (Chambon et al.) (**Exhibit 9**) (An English language counterpart appears in **Exhibit 8**);
10. European Patent Application No. 0 250 997, published July 1, 1988 (Chiesi et al.) (**Exhibit 10**);
11. European Patent Application No. 0 442 012, published August

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21, 1991, (Friedman et al.) (**Exhibit 11**);

12. European Patent Application No. 0 659 174, published October 2, 1999 (Bialer et al.) (**Exhibit 12**);

13. French Patent Application No. 2 531 950, published August 19, 1983 (Cordi et al.) (**Exhibit 13**);

14. Great Britain Patent No. 2 126 224, published March 21, 1984 (Cordi et al.) (**Exhibit 14**);

15. Soviet Union Patent Application No. 988188, published January 7, 1983 (**Exhibit 15**);

16. PCT International Application PCT/US87/02347 (WO 88/01861), published March 24, 1988 (Cotter et al.) (**Exhibit 16**);

17. Bialer, "Clinical Pharmacology of Valpromide", Clinical Pharmacokinet., 1991, 20(2): 114-122 (**Exhibit 17**);

18. Bialer et al., "Pharmacokinetics of a Valpromide Isomer, Valnoctamide, in Healthy Subjects", Eur. J. Clin. Pharmacol., 1990, 38:289-291 (**Exhibit 18**);

19. Buzzi et al., "The Antimigraine Drug, Sumatriptan (GR43175), Selectively Blocks Neurogenic Plasma Extravasation from Blood Vessels in Dura Mater", Brit. J. Pharmacol., 1990, 99: 202-206 (**Exhibit 19**);

20. Granneman et al., "Aspects of the Metabolism of Valproic

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Acid", Chem. Abstracts, 1984, 101(17): 143458 (**Exhibit 20**);

21. Granneman, "Aspects of the Metabolism of Valproic Acid", Xenobiotica, 1984, 14(5): 375-387 (**Exhibit 21**);

22. Hadad et al., "Pharmacokinetic Analysis of Ester Prodrugs of Valproic Acid," J. Pharm. Sci., 1992, 81(10): 1047-1050 (**Exhibit 22**);

23. Haj-Yehia et al., "Structure-Pharmacokinetic Relationships in a Series of Valpromide Derivatives with Antiepileptic Activity", Pharm. Research, 1989, 6(8): 683-689 (**Exhibit 23**);

24. Kim et al., "An Experimental Model for Peripheral Neuropathy Produced by Segmental Spinal Nerve Ligation in the Rat", J.M. Pain, 1992, 50: 355-363 (**Exhibit 24**);

25. March, Advanced Organic Chemistry, 3<sup>rd</sup> Edition, 1985, 354-355, 368, 377-379 (**Exhibit 25**);

26. Yu et al., "Simultaneous Delivery of Valproic Acid and Glycine to the Brain", Neuropath., 1991, 15(1): 37 (**Exhibit 26**);

27. "Milacemide", Drugs of the Future, 1984, 9(8): 587-588 (**Exhibit 27**); and

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28. "Milacemide", Drugs of the Future, 1991, 16(8): 775  
(**Exhibit 28**).

Applicants note that References No. 4-6 were cited in the February 6, 2002 International Search Report in the corresponding PCT International Application and a copy of the Report is enclosed as **Exhibit B**. Applicants request that the Examiner review the publications and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

John P. White  
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Date  
4/15/02